

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A composition for generating a complex-forming metal ion labeled ~~agent~~ conjugate, the composition comprising:

- (a) a metal support surface which is made of gold, silver or copper, or which is a substrate that is coated with gold, silver or copper, said substrate selected from the group consisting of inorganic silicate glass, alkylamino functionalized controlled-pore glass, silica, alumina beads, organic polystyrene, polyacrylamide, Sephadex, and agarose; and
- (b) a conjugate releasably bound to the support surface, the conjugate comprising a ligand and a targeting molecule;

wherein the conjugate coordinates with a complex-forming metal ion so that the labeled conjugate is released from the support surface.

2. (Previously presented) The composition of claim 1, wherein the metal support surface releasably coordinates to sulfur or phosphorous and the ligand comprises a sulfur or phosphorous atom for binding to the metal support surface.

3. (Previously presented) The composition of claim 2, wherein the ligand comprises a sulfur atom attached to a sulfur protecting group, wherein the metal support surface binds to the protected sulfur atom thereby releasing the sulfur protecting group from the sulfur atom and forming a thiol bond with the ligand.

4. (Currently amended) The composition of claim 2, wherein the ~~conjugate~~ targeting molecule comprises a peptide, a polypeptide, a peptide or polypeptide mimetic or an organic molecule having a molecular weight less than about 600 Daltons.

5. (Currently amended) The composition of claim 4, wherein the ~~conjugate~~ targeting molecule comprises a peptide sequence selected from the group consisting of a bombesin 7-14 fragment, QWAVGHLM (SEQ ID NO:1), TKPPR (SEQ ID NO:2) and RGDS (SEQ ID NO:3).

6. (Currently amended) The composition of claim 4, wherein the ~~conjugate~~ targeting molecule comprises a small organic molecule that targets a receptor or a transporter.

7. (Currently amended) The composition of claim 2, wherein the ligand comprises:

(a) a surface binding group selected from the group consisting of a cysteine amino acid residue, a thiol or thioester group attached to an organic molecule, an amino acid residue, and a phosphorous containing organic molecule, wherein the amino acid residue or organic molecule binds to the support surface; and

(b) at least one accessory group that coordinates with the complex-forming metal ion, where the accessory group is selected from the group consisting of (a) a nitrogen, oxygen or sulfur atom incorporated in an amino acid residue; (b) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an amino acid residue; (c) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an organic molecule; and (d) a combination of one or more of (a) to (c), wherein the residues and/or molecules have metal coordinating activity.

8. (Currently amended) The composition of claim 7, wherein the ~~ligand~~ targeting molecule comprises a peptide, a peptide mimetic, a polypeptide, a polypeptide mimetic or an organic molecule having a molecular weight less than about 600 Daltons.

9. (Currently amended) The composition of claim 8, wherein the ligand comprises a peptide selected from the group consisting of a tetradentate ~~N₄S₄~~ N₃S ligand, and a polyamino polysulfide.

10. (Currently amended) The composition of claim 8, wherein the ~~ligand~~ targeting molecule comprises 3 accessory groups, each selected from the group consisting of (a) a nitrogen, oxygen or sulfur atom incorporated in an amino acid residue; (b) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an amino acid residue; (c) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an organic molecule; and (d) a combination of one or more of (a) to (c), wherein the residues and/or molecules have metal coordinating activity.

11. (Previously presented) The composition of claim 1, wherein the targeting molecule comprises a molecule having agonist or antagonist activity selected from the group consisting of a polypeptide, a peptide, a nucleic acid molecule, an oligonucleotide, a saccharide, an oligosaccharide, a steroid, a cyclic peptide, a peptide or polypeptide mimetic, an enzyme substrate, an inhibitor and an organic molecule having a molecular weight less than about 600 Daltons.

12. (Previously presented) The composition of claim 1, wherein the targeting molecule comprises a peptide, a polypeptide, a peptide or polypeptide mimetic or an organic molecule having a molecular weight less than about 600 Daltons.

13. (Previously presented) The composition of claim 1, wherein the targeting

molecule comprises a molecule selected from the group consisting of a bombesin 7-14 fragment, QWAVGHLM (SEQ ID NO:1), TKPPR (SEQ ID NO:2), RGDS (SEQ ID NO:3) and an organic molecule having a molecular weight less than about 600 Daltons that targets a receptor or a transporter.

14. (Currently amended) The composition of claim ~~6~~ 5 or claim 13, wherein the receptor or transporter is selected from the group consisting of a dopamine receptor or transporter, a serotonin receptor or transporter, a sigma receptor, GABA receptor, a nicotinic receptor, a cholinergic receptor, a norepinephrine receptor or transporter, a glucose transporter and an opioid receptor.

15. (Cancelled)

16. (Currently amended) The composition of claim 3, wherein the metal support surface ~~comprises~~ is gold.

17. (Previously presented) The composition of claim 1, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.

18. (Previously presented) The composition of claim 17, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Cu and Re.

19. (Currently amended) A method ~~for~~ of generating a complex-forming metal ion labeled conjugate for use as a diagnostic agent or radiotherapeutic agent, comprising: ~~(a) providing a composition according to claim 1; and (b) contacting the composition of claim 1 with the a complex-forming metal ion to form a coordinate bond between the complex-forming metal ion and the agent conjugate so that the complex-forming metal labeled agent conjugate is~~

released from the support surface.

20. (Currently amended) The method of claim 19, further comprising collecting the ~~complex-forming metal labeled agent so~~ labeled conjugate released.

21. (Currently amended) A metal ion labeled ~~agent~~ conjugate prepared using a composition of claim 1.

22. (Currently amended) A technetium or rhenium labeled ~~agent~~ conjugate prepared using a composition of claim 1, wherein the ~~agent~~ conjugate is labeled with ^{99m}Tc and has a specific activity of greater than 10,000 Ci/mmol or ~~the agent is labeled with~~ ^{188}Re and has a specific activity of greater than 3,000 Ci/mmol.

23. (Currently amended) The composition of claim 22, wherein the ~~agent~~ conjugate comprises is a peptide comprising dimethylglycylserinylcysteinylglycine.

24. (Currently amended) A pharmaceutical composition ~~for radiotherapy or imaging,~~ comprising a pharmaceutically acceptable carrier and ~~the a complex-forming~~ metal ion labeled ~~agent, wherein the agent is prepared using a composition of claim 1.~~ conjugate of claim 21.

25. (Original) The pharmaceutical composition of claim 24 further comprising at least one agent selected from the group consisting of a reducing agent, a bulking agent and a pH stabilizing agent.

26. (Currently amended) A method of ~~detecting the presence or assessing the severity of an oncological, neurological, inflammatory, infectious and degenerative disease, disorder or abnormal physical state in~~ imaging a mammal comprising:

- (a) administering an effective amount of the ~~agent or~~ composition of ~~claim 22 or~~ claim 24; and
- (b) ~~detecting the presence or assessing the severity of the disease,~~

~~disorder or abnormal physical state.~~ generating an image.

27. (Currently amended) A method of radiotherapy ~~of a disease, disorder or abnormal physical state~~ in a mammal comprising administering an effective amount of the agent ~~or composition of claim 22 or claim 24.~~

28. (Currently amended) The method of claim 26, wherein the ~~complex-forming metal labeled imaging agent composition~~ is administered ~~by an intravenous route.~~ intravenously.

29. (Cancelled)

30. (Cancelled)

31. (Previously presented) The method of claim 26, wherein the mammal is a human.

32. (Cancelled)

33. (Currently amended) The method of claim 26, wherein the ~~presence or the severity of a disease, disorder or abnormal physical state is detected or assessed with~~ mammal is imaged by a technique selected from the group consisting of positron emission tomography, nuclear magnetic resonance imaging, scintigraphy, single photon emission computed tomography, perfusion contrast echocardiography, ultrafast X-ray computed tomography, and digital subtraction angiography.

34. (Currently amended) The method of claim 33, wherein the ~~agent comprises a ^{99m}Tc metal and binds to a receptor and the~~ technique is single photon emission computed tomography.

35. (Currently amended) A kit ~~for preparing a complex-forming metal ion labeled agent, the kit~~ comprising a metal support surface, conjugate and a predetermined quantity of complex-forming metal ion, the conjugate being releasably bound to the support surface and which coordinates with the complex-forming metal ion so that the conjugate is released from the

metal support surface,

wherein said metal support surface is made of gold, silver or copper, or is a substrate that is coated with gold, silver or copper, said substrate selected from the group consisting of inorganic silicate glass, alkylamino functionalized controlled-pore glass, silica, alumina beads, organic polystyrene, polyacrylamide, Sephadex, and agarose and the conjugate comprises a ligand and a targeting molecule.

36. (Currently amended) The kit of claim 35, wherein the ~~conjugate~~ ligand comprises a sulfur atom attached to a sulfur protecting group, ~~wherein the metal support surface binds to the protected sulfur atom thereby releasing the sulfur protecting group from the sulfur atom and forming a thiol bond with the conjugate.~~

37. (Currently amended) The kit of claim 35, wherein the ~~metal support~~ ligand ~~surface releasably coordinates to sulfur or phosphorous and the conjugate~~ comprises a sulfur or phosphorous atom for binding to the metal support surface.

38. (Currently amended) The kit of claim 27, wherein the conjugate comprises a ligand and a targeting molecule, wherein the ligand comprises:

- (a) a surface binding group selected from the group consisting of a cysteine amino acid residue, a thiol or thioester group attached to an organic molecule having a molecular weight less than about 600 Daltons, and a phosphorous containing organic molecule, wherein the amino acid residue or organic molecule releasably binds to the support surface; and
- (b) at least one accessory group that coordinates with the complex-forming metal ion wherein the accessory group is selected from the group

consisting of (a) a nitrogen, oxygen or sulfur atom incorporated in an amino acid residue; (b) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an amino acid residue; (c) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an organic molecule; and (d) a combination of one or more accessory groups.

39. (Previously presented) The kit of claim 35, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.

40. (Previously presented) The kit of claim 39, further comprising at least one agent selected from the group consisting of a reducing agent, a bulking agent and a pH stabilizing agent.

41. (Previously presented) A method for generating a complex-forming metal ion labeled agent comprising:

(a) providing a metal support surface which is made of gold, silver or copper, or which is a substrate that is coated with gold, silver or copper, said substrate selected from the group consisting of inorganic silicate glass, alkylamino functionalized controlled-pore glass, silica, alumina beads, organic polystyrene, polyacrylamide, Sephadex, and agarose;

(b) providing a conjugate comprising a ligand and targeting molecule, wherein the ligand comprises a peptide, a peptide mimetic, a polypeptide or a polypeptide mimetic of about 3 to 50 amino acid residues and includes a sulfur atom for binding to the metal support surface, the sulfur atom being protected by a sulfur protecting group;

(c) contacting the protected sulfur atom with the metal support surface so that the sulfur atom forms a thiol bond with the metal surface thereby releasing the sulfur protecting group; and

(d) contacting the ligand with the complex-forming metal ion to form a coordinate bond between the complex-forming metal ion and the ligand so that the complex-forming metal labeled agent is released from the support surface.

42. (Previously presented) The method of claim 41, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.

43 - 44. (Cancelled)

45. (Currently amended) The composition of claim 1, wherein the ligand comprises an organic molecule having a molecular weight of less than about 600 Daltons, which comprises:

(a) a sulfur atom in the form of a thiol or thioether group or a phosphorous atom where the sulfur or phosphorous atom binds to the support surface; and

(b) at least one accessory group that coordinates with the complex-forming metal ion wherein the accessory group is selected from the group consisting of (a) a nitrogen, oxygen or sulfur atom incorporated in an amino acid residue; (b) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an amino acid residue; (c) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an organic molecule; and (d) a combination of one or more accessory groups.

46. (Currently amended) The kit of claim ~~27~~ 37, wherein the conjugate comprises a

ligand and a targeting molecule, wherein the ligand comprises an organic molecule having a molecular weight of less than about 600 Daltons, which comprises:

(a) a sulfur atom in the form of a thiol or thioether group or a phosphorous atom where the sulfur or phosphorous atom binds to the support surface; and

(b) at least one accessory group that coordinates with the complex-forming metal ion wherein the accessory group is selected from the group consisting of (a) a nitrogen, oxygen or sulfur atom incorporated in an amino acid residue; (b) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an amino acid residue; (c) a nitrogen, oxygen, selenium, phosphorous or sulfur atom incorporated in an organic molecule; and (d) a combination of one or more accessory groups.

47-49 (Cancelled)